REMARKS

Claims 16, 17, 24–55, 57-58, 60, 62, 64, and 68-78 are now pending in the present application, of which Claims 16, 36 and 68–77 are presently withdrawn from consideration. Claims 1-15 and 18–23 were previously cancelled. By present amendment, Claims 56, 59, 61, 63, and 65-67 are cancelled.

Claims 35, 58, 60, 62, and 64 are amended herein to each include a *Markush* group of additional active ingredients. Support is found in the specification as filed, at least at paragraphs **[0054]**, **[0055]**, and **[0059]-[0062]**.

No new matter is added, and no change in inventorship is believed to result from the present amendment.

RESPONSE TO OFFICE ACTION DATED 7 DECEMBER 2009

1. Non-statutory double patenting

Claims 17, 24-35, and 37–67 are provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly unpatentable over Claims 10–82 of copending application Serial No. 10/565,699 ("the '699 application").

Applicant again notes that presently amended Claim 17 is directed to a method of treating depression in a mammal by administering to the mammal a therapeutically effective amount of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol or a physiologically acceptable salt thereof. Claim 17 is not limited to a "method of treating depression comprising administering compounds including rotigotine (elected species) and additional drugs that include antidepressants, antipsychotics, anxiolytics, anti-migraine [agents] and sedatives" as implied in the Action (p. 3). Furthermore, Claims 10-82 of the '699 application are not all directed to method of treating depression by administering rotigotine and an additional drug.

Second, the rejection is provisional because the allegedly conflicting claims have not yet been patented. Applicant may elect to argue to overcome this ground of rejection or to provide a terminal disclaimer (to the extent necessary) once the present claims have been found to be otherwise allowable and/or once the '699 application issues as a patent.

2. Rejection under 35 U.S.C. §112, first paragraph

Claims 17, 35, and 56–67 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to meet the enablement requirement. This rejection is moot with respect to now cancelled Claims 56, 59, 61, 63, and 65-67 and is respectfully traversed with respect to Claims 17, 35, 57-58, 60, 62, and 64.

The Action (p. 4) again asserts that the specification "while demonstrating the suitability of rotigotine as an antidepressant in three animal models ... does not reasonably provide enablement for treating depression in a combination therapy as claimed...with addition of one or more antidepressants, anxiolytics, sedatives, antipsychotics and anti-migraine agents." Presently amended Claims 35, 58, 60, 62, and 64 each focus on administering 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol or a salt thereof and a *Markush* group of additional active ingredients. Applicant submits that the specification as filed, including the data for treatment of depression with rotigotine (the (S)-enantiomer of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol) and the data known in the art regarding the additional active ingredients fully enables the claims (and those that depend therefrom).

Taking each of the Wands factors in turn, Applicant responds as follows.

Nature of the Invention and Breadth of Claims: At the outset, Applicant states that Claim 14 is a dependent claim directed to different administration routes, and Claim 14 was cancelled by preliminary amendment at the time of filing in the United States.

Claim 17 (what Applicant assumes the Office Action meant to note) is focused on administering 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol or a salt thereof. The Office Action (bridging p. 5-6) asserts that "Claims 35, 56-65 are very broad with respect to the addition of another ingredient in the treatment namely antidepressants (from various classes), sedatives, anti-psychotics, anti-migraine and anxiolytics compounds." Dependent Claim 35 is amended herein to recite specific classes of antidepressants. Further, Claims 58, 60, 62, and 64 are amended herein to each include a *Markush* group of specific additional active ingredients, rather than a broader recitation of a class of compounds. Furthermore, based on the disclosure in the specification and knowledge of one of ordinary skill in the art, Applicant submits Claims 17, 35, 37-58, 60, 62 and 64 are not broader than

what is enabled by the specification as filed for at least the reasons below.

The Relative Skill of Those in the Art. Applicant agrees that the relative skill of those in the art is "high."

The State of the Prior Art and the Predictability of the Art: Applicant agrees that, at the time of invention, it was unpredictable whether rotigotine would be effective in treating depression. Likewise, at the time of invention, it was "not possible to predict that rotigotine can be combined with other antidepressants, (from various classes), sedatives, anti-psychotics, anti-migraine and anxiolytics compounds in treating depression and be therapeutically effective." Applicant agrees that the prior art does not disclose administering rotigotine alone or in combination to treat depression. However, Applicant's invention disclosure enables one of ordinary skill in the art not to find it "highly unlikely" that rotigotine alone or in combination can treat depression effectively (*i.e.* one of ordinary skill in the art now understands from Applicant's disclosure that rotigotine alone or in combination can effectively treat depression).

Guidance of the Specification: The Office Action (p. 7) states that "[t]he specification does not provide any combination therapy with rotigotine or any of the compounds claimed with any additional ingredients claimed in the treatment." Applicant respectfully disagrees. At paragraph **[0056]**, the specification as filed teaches that "[d]epending on the cause and the symptoms of the depression, a combination preparation may also contain an additional antipsychotic, sedative, anxiolytic, or anti-migraine agent, or an active ingredient which displays one or more effects selected from an antidepressive, antipsychotic, sedative, anxiolytic or anti-migraine effect." Furthermore, at paragraphs **[0053]**-**[0055]** and **[0059]**-**[0062]**, the specification as filed identifies specific exemplar antipsychotic, sedative, anxiolytic, or anti-migraine agents. The specification provides guidance as to administration of "the compound of formula I and the additional antidepressant, antipsychotic, sedative, anxiolytic, or anti-migraine agents at paragraphs **[0057]** and **[0058]**. Furthermore, the specification as filed at paragraph **[0052]** teaches that "in one embodiment of the invention, other active ingredients in addition to compounds of formula I may also be present in the antidepressive medicament form." Thus, the specification as filed teaches one of ordinary skill in art classes of exemplar additional active ingredients, exemplar compounds within

those classes and exemplar administration routes and medicament forms.

The Office Action (p. 7) also states that "[t]he specification does not provide any guidance of how much dosage is effective of each additional antidepressant or sedative or anxiolytic or anti-migraine or anti-psychotic in combination therapy in any of the compounds listed." The Examiner has previously stated that "[i]t is well within the [art of the] skilled medical professional to determine suitable dosing regimens." *See* Office Action dated 7 April 2009, at p. 17. It follows from this admission and from the present disclosure, enablement exists for one of ordinary skill in the art to treat depression by administering a therapeutically effective amount of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol in combination with one or more additional active ingredients having an antidepressive, antipsychotic, sedative, anxiolytic or anti-migraine effect." *See* the specification as filed at paragraph **[0056]**.

Working Examples. Contrary to the Examiner's statement at p. 8, one of ordinary skill in the art would not have to engage in undue experimentation, as Claims 58, 60, 62, and 64 as amended herein recite a *Markush* group, specifying particular additional active ingredients in the class of compounds recited in Claim 35. Each of the additional active ingredients are recognized in the art as having antidepressive, antipsychotic, sedative, anxiolytic or anti-migraine effect. The specification as filed teaches one of ordinary skill in art:

- classes of additional active ingredients,
- compounds within those classes,
- administration forms of the combination therapy (including administration at separate times),
- dosage forms, and
- dosage amounts of formula I.

Therefore, no undue amount of experimentation is necessary to practice the invention as claimed in Claims 35, 58, 60, 62, and 64.

In summary, a correct analysis under *In re Wands* leads to the conclusion that treatment of depression by administering 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol, or a salt thereof, alone or in combination with an additional

therapeutic agent as set forth in Claims 35, 58, 60, 62, and 64, is fully enabled by the specification under 35 U.S.C. §112, first paragraph.

Withdrawal of the present rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

3. Rejection under 35 U.S.C. §103(a) over the Alleged 4-Way Combination of Van der Weide, Andersson and Sherman in view of Lauterbach

Claims 17, 24-34, 37-55, and 78 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over an alleged combination of 4 documents: Van der Weide *et al.* (1988) Eur. J. Pharmacol. 146:319–326 ("Van der Weide"), European Patent Publication No. 0 334 538 ("Andersson") and Sherman (2001) Clinical Psychiatry News, Nov. 1, 2001 ("Sherman") in view of International Publication No. WO 02/089777 ("Lauterbach"). This 4-way rejection is respectfully traversed.

3.1. No Disclosure or Teaching Of 5,6,7,8-tetrahydro-6-[propyl-[2-(2 thienyl)ethyl]amino]-1-naphthol To Treat Depression

The Examiner asserts (p. 20):

> Weide et al. teaches enantiomers of N-0437 (rotigotine), d2 dopamine receptor agonists stimulates presynaptic dopamine receptors and blocks postsynaptic receptors and these properties make the enantiomers of N-0437 very promising candidates for psychotherapeutic use.

This summary of Van der Weide is inaccurate. At the outset (and despite Applicant's error in identifying (+)N-0437 as rotigotine, p. 17 of the Office Action Response dated 7 August 2009), (-)N-0437 is synonymous with rotigotine. Furthermore, despite the abstract reporting that Van der Weide concludes that (+) and (-)N-0437 may be "promising candidates for psychotherapeutic use", in actuality Van der Weide (p. 320) "compared the effects of the (+) and the (-) enantiomers of N-0437 and only:

- speculated that (+)N-0437 could have possible therapeutic application in schizophrenia (p. 324, 2nd column) as opposed to (-)N-0437; and
- speculated that (-)N-0437 (rotigotine) could be a candidate for treating Parkinson's disease (p. 324, 2nd column).

Van der Weide is completely silent regarding whether (1) the racemate (N-0437 a.k.a. 5,6,7,8-

tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol) or (2) (-)N-0437 (rotigotine) would be effective in treating schizophrenia or any other "psychotherapeutic use". Thus, the Examiner is reading facts into Van der Weide that are simply not there. In fact, Van der Weide could be seen as teaching away from both the claimed racemate and the (-) enantiomer (rotigotine), because why would one of ordinary skill in the art try the racemate or the (-) enantiomer for depression when Van der Weide speculates that only the (+) enantiomer may be used to treat schizophrenia?

Andersson does not teach the claimed compounds and Sherman reports on pramipexole, not 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol. Lauterbach reports on the measured effects of rotigotine only on Parts II and III of the Unified Parkinson's Disease Rating Scale (UPDRS). Depression is only one aspect of behavior and mood included in Part I of the UPDRS. However, Lauterbach does not teach that rotigotine has effective anti-depressive properties. Thus, none of the cited documents, alone or in combination, teach or suggest that 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol, much less rotigotine, is effective in treating depression.

3.2. No Reasonable Expectation of Success Existed That 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol Effectively Treats Depression

Even if a rationale existed to select and modify elements from the cited documents (which is not admitted herein), the Examiner appears to be applying the "obvious to try" standard in making the present rejection. This standard has been sanctioned by *KSR International Co. v. Teleflex Inc.,* 127 S.Ct. 1727, 82 USPQ2d 1385 (2007), but with the proviso that there has to be "a finite number of identified, predictable solutions" (emphasis added).

Even if, *arguendo,* the compounds reported in Andersson and Sherman are similar to the presently recited 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol, neither Andersson nor Sherman, nor a combination thereof (including Lauterbach and Van der Weide), renders instant Claim 17 obvious. Since the art is admittedly "so highly unpredictable", one of ordinary skill in the art would not predict therapeutic effectiveness of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol in depression just from mention of "similar" structured compounds being effective in treating depression, nor from

the speculative comment in Van der Weide regarding the potential effectiveness of (+)N-0437 for use in schizophrenia (not depression).

The Examiner (p. 22) alleges that since Andersson and Sherman teach similar compounds for the treatment of depression, it would have been obvious to use rotigotine, a known D_2 agonist, to treat depression. However, one of ordinary skill in the art would have had to first pick a compound considered to act on at least one dopamine receptor, then choose one that acted on at least the D_2 receptor, select D_2 agonists, and then select 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol from a number of potential dopamine agonists having completely different structures and therefore, completely different chemical, physical and pharmaceutical properties. This selection process, without any pattern of preference or guidance from the cited documents, would involve:

(1) Review of approximately 169 compounds that can act on dopamine receptors;

(2) Narrowing to approximately 128 compounds that are D_2 receptor acting compounds;

(3) Selecting approximately 30 compounds that are either D_2 agonists or partial agonists;

(4) Testing at least the 30 D_2 agonists or partial agonist compounds; and

(5) Finally, choosing 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol to treat depression.

Accordingly, even if Andersson and Sherman provide "similar" compounds, there is no pattern of preference for specifically choosing 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol, much less rotigotine. At best, the very large number of possible compounds (128 D_2 acting compounds, with at least 30 being D_2 agonists or partial agonists) in combination with the speculative comment in Van der Weide, provides an invitation to "try" or "experiment" on the large number of D_2 agonists, which would include 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol. Such invitation to "try" or "experiment" is not enough to establish a presumption of *prima facie* obviousness. *See Procter & Gamble Co. v. Teva Pharmaceuticals USA, Inc.*, 566 F.3d 989 (Fed. Cir. 2009) (holding that US Patent No. 4,761,406 ("the '406 patent"), which disclosed the compound 2-pyr EHDP, did not render the claims of U.S. Patent No. 5,583,122, reciting the compound

risedronate, obvious, despite risedronate and 2-pyr EHDP being positional isomers of each other).

Each of Claims 24-34, 37-55, and 78 is nonobvious over the 4-way rejection, Van der Weide, Andersson and Sherman in view of Lauterbach, for at least the same reasons that Claim 17 is nonobvious. Withdrawal of the present rejection under 35 U.S.C. §103(a) over Van der Weide, Andersson and Sherman in view of Lauterbach is respectfully requested.

4. Rejection under 35 U.S.C. §103(a) over the Alleged 5-Way Combination of Van der Weide, Andersson and Sherman in view of Lauterbach and Maj

Claims 35, 56, 57, 66 and 67 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over 5 documents: Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of U.S. Patent No. 6,255,329 ("Maj"). This 5-way rejection is respectfully traversed.

For a complete response to the current Office Action, Applicant repeats its response to the rejection. Claims 35 and 57 depend from Claim 17 and further include administering to a mammal an additional active ingredient, such as an antidepressant. For the reasons set forth above, a presumption of *prima facie* obviousness of Claim 17 (and thus of any claim dependent therefrom) over Van der Weide, Andersson and Sherman in view of Lauterbach is not sustainable. Addition of Maj to the previous 4-way combination of documents does not change this conclusion. Maj is cited for disclosure of a combination of pramipexole and sertraline. Thus, the fact remains that 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol was not known to effectively treat depression prior to the present invention.

Furthermore, the Examiner asserts that "[i]t is not possible to predict that rotigotine can be combined with other antidepressants, (from various classes), sedatives, anti-psychotics, anti-migraine and anxiolytics compounds in treating depression and be therapeutically effective." See Office Action, p. 6, lines 3-5. Thus, at the time of invention, it was not possible to predict, in view of the prior art, the effectiveness of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol in combination with an additional active ingredient, specifically an antidepressant. By failing to establish predictability in the claimed invention, the Office Action further fails to establish a presumption of *prima facie* obviousness of

Claims 35 and 57.

Withdrawal of the present 5-way 35 U.S.C. §103(a) rejection of Claims 35 and 57 over Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Maj is respectfully requested. Furthermore, by present amendment Claims 56, 66 and 67 are cancelled, and thus, such rejection is moot.

5. Rejection under 35 U.S.C. §103(a) over the Alleged 5- Way Combination of Van der Weide, Andersson and Sherman in view of Lauterbach and Hrdlička

Claims 58 and 59 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over 5 documents: Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Hrdlička (2002) Eur. Psychiatry 17:484 ("Hrdlička"). This rejection is respectfully traversed.

For a complete response to the current Office Action, Applicant repeats its response to the rejection. Claim 58 depends from Claim 17 (Applicant assumes that mention of Claim 14 in the Office Action, at p. 15, is a typographical error), and further includes administering to the mammal one of the specifically claimed antipsychotics. For the reasons set forth above, a presumption of *prima facie* obviousness of Claim 17 (and thus of any claim dependent therefrom) over Van der Weide, Andersson and Sherman in view of Lauterbach is not sustainable. Addition of Hrdlička to the previous 4-way combination of documents does not change this conclusion. Hrdlička is cited for disclosure of a one-patient study of a combination of clozapine and maprotiline. Thus, the fact remains that 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol was not known to have antidepressant activity prior to the present invention, therefore the cited art fails to teach or suggest the invention as claimed in Claim 58. The Action mentions Timmerman *et al.* (1990) Eur. J. Pharmacol. 181:253–260 as remarking that "(+)N-0437 is a possible candidate for therapeutic use in schizophrenia"; however, this document does not appear to be applied in the present rejection and the recited disclosure appears in any case to be merely cumulative over that of Van der Weide.

Furthermore, the Examiner asserts that "[i]t is not possible to predict that rotigotine can be combined with other antidepressants, (from various classes), sedatives, anti-psychotics,

anti-migraine and anxiolytics compounds in treating depression and be therapeutically effective." See Office Action, p. 6, lines 3-5. Thus, at the time of invention, it was not possible to predict, in view of the prior art, the effectiveness of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol in combination with an additional active ingredient, specifically an antipsychotic. By failing to establish predictability in the claimed invention, the Office Action further fails to establish a presumption of *prima facie* obviousness.

Withdrawal of the present 5-way 35 U.S.C. §103(a) rejection of Claim 58 over Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Hrdlička is respectfully requested. Furthermore, by present amendment, Claim 59 is cancelled, and thus, such rejection is moot.

6. Rejection under 35 U.S.C. §103(a) over the Alleged 5-Way Combination of Van der Weide, Andersson and Sherman in view of Lauterbach and Kupfer

Claims 60 and 61 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over 5 documents: Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Kupfer (1999) Ann. Clin. Psychiatry 11:267–276 ("Kupfer"). This rejection is respectfully traversed.

For a complete response to the current Office Action, Applicant repeats its response to the rejection. Claim 60 depends from Claim 17 (Applicant assumes that mention of Claim 14 in the Office Action, at p. 16, is a typographical error) and is drawn to a method of Claim 17 that further includes administering to the mammal one of the specifically claimed sedatives. For the reasons set forth above, a presumption of *prima facie* obviousness of Claim 17 (and thus of any claim dependent therefrom) over Van der Weide, Andersson and Sherman in view of Lauterbach is not sustainable. Addition of Kupfer to the combination of documents does not change this conclusion. Kupfer is cited for the disclosure that depression can be accompanied by insomnia. The Action mentions U.S. Patent Application Publication No. 2002/0177626 as disclosing that diphenhydramine is a sedative, though this document does not appear to be applied in the present rejection. Thus, the fact remains that 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol was not known to have antidepressant activity prior to the present invention, therefore the cited art fails to teach or

suggest the invention as claimed in Claim 60.

Furthermore, the Examiner asserts that "[i]t is not possible to predict that rotigotine can be combined with other antidepressants, (from various classes), sedatives, anti-psychotics, anti-migraine and anxiolytics compounds in treating depression and be therapeutically effective." See Office Action, p. 6, lines 3-5. Thus, at the time of invention, it was not possible to predict, in view of the prior art, the effectiveness of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol in combination with an additional active ingredient, specifically an antipsychotic. By failing to establish predictability in the claimed invention, the Office Action further fails to establish a presumption of *prima facie* obviousness.

Withdrawal of the present 5-way 35 U.S.C. §103(a) rejection of Claim 60 over Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Kupfer is respectfully requested. Furthermore, by present amendment, Claim 61 is cancelled, and thus, such rejection is moot.

7. Rejection under 35 U.S.C. §103(a) over the Alleged 5-Way Combination of Van der Weide, Andersson and Sherman in view of Lauterbach and Zimmerman

Claims 62 and 63 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over 5 documents: Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Zimmerman & Chelminski (2003) Am. J. Psychiatry 160:504–512 ("Zimmerman"). This rejection is respectfully traversed.

For a complete response to the current Office Action, Applicant repeats its response to the rejection. Claim 62 depends from Claim 17 (Applicant assumes that mention of Claim 14 in the Office Action, at p. 17, is a typographical error) and is drawn to a method of Claim 17 that further includes administering to the mammal specifically claimed anxiolytic. For the reasons set forth above, a *prima facie* obviousness of Claim 17 (and thus of any claim dependent therefrom) over Van der Weide, Andersson and Sherman in view of Lauterbach is not sustainable. Addition of Zimmerman to the combination of documents does not change this conclusion. Zimmerman is cited for the disclosure that depression can be accompanied by generalized anxiety disorder (GAD). The Action mentions Lehmann (1989) Neuropsychobiology 21:197–204 as disclosing that fluspirilene is an anxiolytic, though this

document does not appear to be applied in the present rejection. Thus, the fact remains that 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol was not known to have antidepressant activity prior to the present invention, therefore, the cited art fails to teach or suggest the invention as claimed in Claim 62.

Furthermore, the Examiner asserts that "[i]t is not possible to predict that rotigotine can be combined with other antidepressants, (from various classes), sedatives, anti-psychotics, anti-migraine and anxiolytics compounds in treating depression and be therapeutically effective." See Office Action, p. 6, lines 3-5. Thus, at the time of invention, it was not possible to predict, in view of the prior art, the effectiveness of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol in combination with an additional active ingredient, specifically an antipsychotic. By failing to establish predictability in the claimed invention, the Office Action further fails to establish a presumption of *prima facie* obviousness.

Withdrawal of the present 5-way 35 U.S.C. §103(a) rejection of Claim 62 over Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Zimmerman is respectfully requested. Furthermore, by present amendment, Claim 63 is cancelled, and thus, such rejection is moot.

8. Rejection under 35 U.S.C. §103(a) over the Alleged 5-Way Combination of Van der Weide, Andersson and Sherman in view of Lauterbach and Medicine News

Claims 64 and 65 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over 5 documents: Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Anon. (2003) "Links between depression and migraine" www.bio-medicine.org/medicine-news/Links-between-Depression-and-Migraine-2005-1/ ("Medicine News"). This rejection is respectfully traversed.

For a complete response to the current Office Action, Applicant repeats its response to the rejection. Claim 64 depends from Claim 17 (Applicant assumes that mention of Claim 14 in the Office Action, at p. 18, is a typographical error) and is drawn to a method of Claim 17 that further includes administering to the mammal a specifically claimed anti-migraine agent. For the reasons set forth above, a presumption of *prima facie* obviousness of Claim 17 (and thus of any claim dependent therefrom) over Van der Weide, Andersson and Sherman in view of Lauterbach is not sustainable. Addition of Medicine News to the combination of

documents does not change this conclusion. Medicine News is cited for the disclosure that treatments for migraine and major depression can benefit patients with both disorders. The Action mentions U.S. Patent Application Publication No. 2003/0225002 as disclosing that almotriptan is an anti-migraine agent, though this document does not appear to be applied in the present rejection. Thus, the fact remains that 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol was not known to have antidepressant activity prior to the present invention, therefore, the cited art fails to teach or suggest the invention as claimed in Claim 64.

Furthermore, the Examiner asserts that "[i]t is not possible to predict that rotigotine can be combined with other antidepressants, (from various classes), sedatives, anti-psychotics, anti-migraine and anxiolytics compounds in treating depression and be therapeutically effective." See Office Action, p. 6, lines 3-5. Thus, at the time of invention, it was not possible to predict, in view of the prior art, the effectiveness of 5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl)ethyl]amino]-1-naphthol in combination with an additional active ingredient, specifically an antipsychotic. By failing to establish predictability in the claimed invention, the Office Action further fails to establish a presumption of *prima facie* obviousness.

Withdrawal of the present 5-way 35 U.S.C. §103(a) rejection over Van der Weide, Andersson and Sherman in view of Lauterbach and further in view of Zimmerman is respectfully requested. Furthermore, by present amendment, Claim 65 is cancelled, and thus, such rejection is moot.

9. Conclusion

It is believed that all of the stated grounds of rejection are properly traversed, accommodated, or rendered moot herein. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the present Action and that the application is in condition for allowance.

If personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number below.